REMARKS

Applicant acknowledges the election of Group I and the finality of the restrictions requirement. However, claims 12 and 13 were added as new claims following the restriction requirement and it was pointed out to the Examiner that claims 12 and 13 are part of the species of claim 1 since they are directed specifically to the viscous and glassy composition of claim 1. In fact, claim 12 is dependent upon claim 1.

Accordingly, claims 12 and 13 cannot be arbitrarily withdrawn by the Examiner without providing an explanation as to how or why these claims fall into Group II which are drawn to a method or to a separate group. Moreover, the finality cannot apply to new claims added after the restriction requirement. Therefore, the Examiner is requested to cancel the withdrawal as to claims 12 and 13, acknowledge that claims 12 and 13 are part of the elected Group I, and consider them on their merits.

The Examiner's Office Communication dated July 27, 2006 has otherwise been carefully reviewed. However, based upon the attached Declaration under 35 USC132 in connection with the reasons provided below, claims 1-9 and 12-13 are believed to be clearly allowable over the cited prior art.

I. Objections

In view of the informalities in claims 5 to 9 pointed out by the Examiner, claims 5 to have been appropriately corrected to overcome the Examiner's objections.

Therefore, the objections to claims 5 to 9 should be withdrawn.

II. 35 U.S.C. 102 and 103 Rejections

The Examiner has rejected claims 1, 6 and 7 under 35 U.S.C. 102(b) as being anticipated by Baert et al. (WO 97/44014); and claims 1-9 under 35 U.S.C. 103(a) as being unpatentable over Baert et al. in view of Patel et al. (U.S. Patent #6,248,363). These rejections are respectfully traversed.

The present invention as defined in pending claims 1-9 and 12-13 is directed to a viscous and glassy composition for oral administration and comprises: itraconazole, an

acidifying agent, an amphiphilic additive, a surfactant and an oil. All four components must be specifically taught in a cited reference in a rejection under 35 USC 102.

The oral itraconazole composition of the present invention provides a high and stable level rate of itraconazole dissolution even under a neutral or alkaline condition at a pH of 6.8 or higher, and the itraconazole bioavailability is little influenced by ingested food. In other words, the bioavailability of itraconazole in the inventive composition is almost the same both before and after ingestion.

i) Summary of cited references

The Baert patent cited as a primary reference discloses a solid in a dispersion comprising (a) itraconazole, its stereoisomers, or a mixture thereof, and (b) one or more pharmaceutically acceptable water-soluble polymers (e.g., hydroxypropylmethylcellulose (HPMC)) (see claims 1 and 5). Further, the Baert patent teaches itraconazole, HPMC, propylene glycol, hydrogenated vegetable oil and the like as constituents of a preferred oral composition (see line 25, page 12 to line 4, page 13). Baert also teaches that itraconazole may be present in the form of an acid addition salt generated by reaction with an appropriate acid (see line 34, page 1 to line 4, page 2).

The Patel patent is cited as a secondary reference, and is directed to a solid carrier for improved delivery of active ingredients in pharmaceutical compositions. Patel teaches various additives such as anti-adherents, anticoagulants, antifoaming agents, antioxidants, binders, bufferants and the like which may be conventionally employed in pharmaceutical compositions, wherein silica and tocopherol are exemplified as one of the anti-adherents and antioxidants, respectively (see lines 15-30, page 39).

ii) Rejection under 35 U.S.C. 102 –
Comparison of the present invention with the Baert patent

The Examiner has pointed out that "HPMC", "propylene glycol", "hydrogenated vegetable oil" and "acid" disclosed in the Baert patent correspond to "a surfactant", "an amphiphilic additive", "an oil" and "an acidifying agent" employed in the inventive composition,

respectively, and therefore, the novelty step of the instantly claimed composition is lacking.

Contrary to the allegations of the Examiner, the composition, as claimed, is entirely different from that taught in the Baert patent not only in constituent composition, but also in terms of its form, phase and function, as discussed below:

A) Constituents

The itraconazole composition of the subject invention as claimed comprises an acidifying agent, an amphiphilic additive, a surfactant and an oil. All are essential constituents, whereas the itraconazole composition in the Baert patent does not comprise "an acidifying agent" or "a surfactant." For this reason alone, the rejection under 35 USC 102 is not applicable.

More specifically, first, the inventive composition comprises itraconazole and an acidifying agent for dissolving itraconazole as two separate components, wherein the acidifying agent is substantially used as a mixture with other ingredients including the amphiphilic additive in the preparation of the composition (see lines 12-16 and 30-35, page 3 of the inventive specification). The use of itraconazole and an acidifying agent as independent components of claim 1 is not satisfied by the teaching of "an acid addition salt of itraconazole" mentioned in the Baert patent.

In addition, the inventive composition comprises a surfactant which possesses both hydrophilic and hydrophobic parts, assisting the formulation of a uniform emulsion of an oil and hydrophilic components, and keeping the emulsion stable during storage (see lines 17-20, page 4 of the inventive specification). In contrast, hydroxypropylmethylcellulose (HPMC) which is employed in Baert is simply just a water-soluble polymer which acts as a carrier and is not a surfactant nor does Baert suggest otherwise.

B. Form, Phase and Function

The itraconazole composition of the subject invention forms "a liquid phase of microemulsion preconcentrate" which is viscous and glassy and is much more compact as compared with a conventional microemulsion composition (see lines 30-35, page 5 of the inventive specification). The inventive composition has self-microemulsifying capability to form highly stable, several to several ten nm-sized microemulsion particles in the body fluid when orally administered (see line 36, page 5 to line 2, page 6 of the inventive specification). The microemulsion thus formed in the body has "a complete spherical shape," the surfactant enveloping all of the components, itraconazole, the acidifying agent, the amphiphilic additive and the oil, and it becomes highly absorbable, especially while passing through a lymphatic pathway, due to its ultrafine size, i.e., nano-size.

In contrast to the viscous and glassy emulsion composition of the subject invention, the Baert composition is "a solid dispersion" (in a solid state as opposed to a viscous state which may be a liquid or gaseous state) in which itraconazole is dispersed evenly throughout a water-soluble polymer carrier (matrix), formed by blending itraconazole and the water-soluble polymer, and then extruding the blend at a temperature in the range of 120 to 300L, followed by grinding the extrudate (see claims 1 and 10, and lines 5-17 and 30-34, page 4 of the Baert's specification).

As described above, it is clear that the composition claimed in the present invention and the teaching in Baert is distinctly different.

Accordingly, the Baert patent fails to anticipate the present invention and the 102 rejection of claims 1, 6 and 7 should be withdrawn.

iii) As to the Rejection under 35 U.S.C. 103

The Examiner alleges that: "Because of the teachings of Patel (both) tocopherol and silica can be used as additives in a similar composition" and that it would have been

obvious to use tocopherol in the composition of Baert because Baert et al teaches the use of silica and that according to Patel both components are additives.

However, in Patel silica and tocopherol have separate functions for use as an anti-adherent and an antioxidant, respectively (see lines 15-30, page 39). Thus, it is submitted that the Examiner's opinion that they are interchangeable additives is inconsistent. Even if it is assumed that silica and tocopherol can be interchangably employed, it should be noted that the composition of the subject invention requires the addition of a surfactant and an acidifying agent (regardless of silica or tocopherol) which is taught in Baert, as set forth above.

Meanwhile, the inventive composition provides improved itraconazole bioavailability which is little influenced by ingested food, as fully supported by Test Examples 1 (dissolution test) and 2 (*in vivo* absorption test) of the specification as originally filed. As can be seen in the results, i.e., Tables 1 and 2, of Test Example 1, the inventive preparation of Example 1 exhibits higher amounts of itraconazole dissolved than those of Comparative Example and the commercially available preparations at pH 1.2 or 6.8, wherein Sporanox® tablet (Janssen Korea) corresponds to the formulation of the composition disclosed in the Baert patent.

To further illustrate and demonstrate the benefit achievable by the present invention, the applicant submits a declaration in accordance with 37 C.F.R. section 1.132 together with this response. This declaration shows the results of a comparative experiment carried out with the inventive preparation of Example 1 and Sporanox® tablet, which illustrate that the compositions of the present invention are clearly superior over those of the Baert patent in terms of the itraconazole bioavailability and the effect of food.

As described above, it is believed that the compositions disclosed in the present invention and cited references are obviously different, and the unique feature of the present invention as well as beneficial effects arising therefrom are not taught, suggested or implied by the cited references, even if they are combined. Accordingly, the present invention as defined in claims 1-9 and 12-13 is clearly patentable and unobvious over the

cited references, and it is respectfully submitted that the rejection of claims 1-9 and 12-13 under 35 USC 103 be withdrawn.

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CONCLUSION

In view of the foregoing amendments and discussions, it is respectfully submitted that the present invention as defined in the pending claims 1 to 9 and 12 to 13 is in full compliance with all the statutory requirements, and, therefore, it is earnestly requested that the Examiner's objections and rejections be withdrawn and the pending claims be allowed in their present form.

Respectfully submitted,

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MAILING CERTIFICATE

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450 on 26 January 2007

Date: 26 Jan '07